CLAIMS

1. A retroviral vector comprising a functional splice donor site (FSDS) and a functional splice acceptor (FSAS) site; wherein the FSDS and the FSAS flank a first nucleotide sequence of interest (NOI); wherein the FSDS is upstream of the FSAS; wherein the retroviral vector is derived from a retroviral pro-vector; wherein the retroviral pro-vector comprises a first nucleotide sequence (NS) capable of yielding the functional splice donor site (FSDS); a second NS capable of yielding the functional splice acceptor site (FSAS); a third NS capable of yielding a non-functional splice donor site (NFSDS); a fourth NS capable of yielding a non-functional splice site (NFSS); wherein the first NS is downstream of the second NS and wherein the third NS and fourth NS are upstream of the second NS; such that after reverse transcription of the retroviral pro-vector at a desired target site the retroviral vector is capable of being spliced.

2. A retroviral vector according to claim 1 wherein the NFSS is a NFSDS.

3. A retroviral vector according to claim 1 wherein the NFSS is a non-functional splice acceptor site (NFSAS).

4. A retroviral vector according to claim 1 or claim 2 or claim 3 wherein the retroviral vector further comprises a second NOI; wherein the second NOI is downstream of the FSAS.

5. A retroviral vector according to claim 4 wherein the retroviral pro-vector comprises the second NOI; wherein the second NOI is downstream of the second NS.

6. A retroviral vector according to claim 4 or claim 5 wherein the second NOI, or the expression product thereof, is or comprises a therapeutic agent or a diagnostic agent.

7. A retroviral vector according to any one of the preceding claims wherein the first NOI, or the expression product thereof, is or comprises any one or more of an agent

conferring selectablity (e.g. a marker element), a viral essential element, or a part thereof, or combinations thereof.

8. A retroviral vector according to any one of the preceding claims wherein the first NS is at or near to the 3' end of a retroviral pro-vector; preferably wherein the 3' end comprises a U3 region and an R region; and preferably wherein the first NS is located between the U3 region and the R region.

9. A retroviral vector according to claim 8 wherein the U3 region and/or the first NS of the retroviral pro-vector comprises an NS that is a third NOI; wherein the NOI is any one or more of a transcriptional control element, a coding sequence or a part thereof.

10. A retroviral vector according to any one of the preceding claims wherein the first NS is obtainable from a virus.

11. A retroviral vector according to claim 10 wherein the first NS is an intron or a part thereof.

12. A retroviral vector according to claim 11 wherein the intron is obtainable from the small t-intron of SV40 virus.

13. A retroviral vector according to any one of the preceding claims wherein the retroviral pro-vector comprises a retroviral packaging signal; and wherein the second NS is located downstream of the retroviral packaging signal such that splicing is preventable at a primary target site.

14. A retroviral vector according to claim 13 wherein the retroviral packaging signal comprises the fourth NS which is a NFSDS.

15. A retroviral vector according to claim 14 wherein the retroviral packaging signal comprises a fourth NS which is a NFSAS.

16. A retroviral vector according to any one of the preceding claims wherein the second NS is placed downstream of the first NOI such that the first NOI is capable of being expressed at a primary target site.

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17. A retroviral vector according to any one of the preceding claims wherein the second NS is placed downstream of the first NOI such that the first NOI is capable of being expressed at a primary target site and the retroviral vector titre is enhanced.

18. A retroviral vector according to any one of the preceding claims wherein the second NS is placed upstream of a multiple cloning site such that one or more additional NOIs may be inserted.

19. A retroviral vector according to any one of the preceding claims wherein the second NS is a nucleotide sequence coding for an immunological molecule or a part thereof.

20. A retroviral vector according to claim 19 wherein the immunological molecule is an immunoglobulin.

21. A retroviral vector according to claim 20 wherein the second NS is a nucleotide sequence coding for an immunoglobulin heavy chain variable region.

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22. A retroviral vector according to any one of the preceding claims wherein the vector additionally comprises a functional intron.

23. A retroviral vector according to claim 22 wherein the functional intron is positioned such that the packaging signal is deleted at a desired target site.

24. A retroviral vector according to claim 23 wherein the retroviral vector is a self-inactivating (SIN) vector.

25. A retroviral vector according to claim 23 wherein the functional intron is positioned so that it is capable of restricting expression of at least one of the NOIs in a desired target site.

26. A retroviral vector according to claim 25 wherein the target site is a cell.

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27. A retroviral vector according to any one of the preceding claims wherein the vector or pro-vector is derivable from a murine oncoretrovirus or a lentivirus

28. A retroviral vector according to claim 27 wherein the vector is derivable from MMLV, MSV, MMTV, HIV-1 or EIAV.

29. A retroviral vector as defined in any one of the preceding claims wherein the retroviral vector is an integrated provirus.

30. A retroviral particle obtainable from a retroviral vector according to any one of the preceding claims.

31. A cell transfected or transduced with a retroviral vector according to any one of claims 1-29 or a retroviral particle according to claim 30.

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32. A retroviral vector according to any one of claims 1-29 or a viral particle according to claim 30 or a cell according to claim 31 for use in medicine.

33. Use of a retroviral vector in any one of claims 1 to 29 or a viral particle according to claim 30 or a cell according to claim 31 for the manufacture of a pharmaceutical composition to deliver one or more NOIs to a target site in need of same.

34. A method comprising transfecting or transducing a cell with a retroviral vector according to any one of claims 1 to 29 or a viral particle according to claim 30 or by use of a cell according to claim 31.

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35. A delivery system for a retroviral vector according to any one of claims 1 to 29 or a viral particle according to claim 30 or a cell according to claim 31 wherein the delivery system comprises one or more non-retroviral expression vector(s), adenoviruse(s), or plasmid(s) or combinations thereof for delivery of an NOI or a plurality of NOIs to a first target cell and a retroviral vector for delivery of an NOI or a plurality of NOIs to a second target cell.

36. A retroviral pro-vector as defined in any one of the preceding claims.

37. Use of a functional intron to restrict expression of one or more NOIs within a desired target cell.

38. Use of a reverse transcriptase to deliver a first NS from the 3' end of a retroviral pro-vector to the 5' end of a retroviral vector such that a functional intron is created upon transduction.

39. A hybrid viral vector system for *in vivo* gene delivery, which system comprises one or more primary viral vectors which encode a secondary viral vector, the primary vector or vectors capable of infecting a first target cell and of expressing therein the secondary viral vector, which secondary vector is capable of transducing a secondary target cell.

40. A hybrid viral vector system according to claim 39 wherein the primary vector is obtainable from or is based on a adenoviral vector and/or the secondary viral vector is obtainable from or is based on a retroviral vector preferably a lentiviral vector.

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41. Use of a hybrid viral vector system according to claim 39 and claim 40 wherein the lentiviral vector has a split-intron configuration.

42. A hybrid viral vector system wherein the lentiviral vector comprises or is capable of delivering a split-intron configuration.

43. A lentiviral vector system wherein the lentiviral vector comprises or is capable of delivering a split-intron configuration.

44. An adenoviral vector system wherein the adenoviral vector comprises or is capable of delivering a split-intron configuration.

45. Vectors or plasmids basd on or obtained from any one or more of the entities presented as pE1sp1A, pCI-Neo, pE1RevE, pE1HORSE3.1, pE1PEGASUS4, pCI-Rab, pE1Rab.

46. A hybrid viral vector system for *in vivo* gene delivery, which system comprises a primary viral vector which encodes a secondary viral vector, the primary vector capable of infecting a first target cell and of expressing therein the secondary viral vector, which secondary vector is capable of transducing a secondary target cell, wherein the primary vector is obtainable from or is based on a adenoviral vector and the secondary viral vector is obtainable from or is based on a retroviral vector preferably a lentiviral vector.

47. A hybrid viral vector system for *in vivo* gene delivery, which system comprises a primary viral vector which encodes a secondary viral vector, the primary vector capable of infecting a first target cell and of expressing therein the secondary viral vector, which secondary vector is capable of transducing a secondary target cell, wherein the primary vector is obtainable from or is based on a adenoviral vector and the secondary viral vector is obtainable from or is based on a retroviral vector preferably a lentiviral vector; wherein the viral vector system comprises a functional splice donor site (FSDS) and a functional splice acceptor site (FSAS); wherein the FSDS and the FSAS flank a first nucleotide sequence of interest (NOI); wherein the FSDS is upstream of the FSAS; wherein the retroviral vector is derived from a retroviral pro-vector; wherein the retroviral pro-vector comprises a first nucleotide sequence (NS) capable of yielding the FSDS; a second NS capable of yielding the FSAS; a third NS capable of yielding a non-functional splice donor site (NFSDS); a fourth NS capable of yielding a non-functional splice site (NFSS); wherein the first NS is downstream of the second NS; and wherein the third NS and fourth NS are upstream of the second NS; such that after reverse transcription of the

retroviral pro-vector at a desired target site the retroviral vector is capable of being spliced.

48. A self-inactivating (SIN) retroviral vector comprising a functional splice donor site (FSDS) and a functional splice acceptor (FSAS) site; wherein the FSDS and the FSAS flank a first nucleotide sequence of interest (NOI); wherein the FSDS is upstream of the FSAS; wherein the retroviral vector is derived from a retroviral pro-vector; wherein the retroviral pro-vector comprises a first nucleotide sequence (NS) capable of yielding the functional splice donor site (FSDS); a second NS capable of yielding the functional splice acceptor site (FSAS); a third NS capable of yielding a non-functional splice donor site (NFSDS); a fourth NS capable of yielding a non-functional splice site (NFSS); wherein the first NS is downstream of the second NS and wherein the third NS and fourth NS are upstream of the second NS; such that a retroviral vector cannot be packaged as a result of reverse transcription of the retroviral pro-vector at a target site.

49. A retroviral vector capable of differential expression of NOIs in target cells substantially as described herein.